NATIONAL MARROW DONOR PROGRAM®

Advances in Conditioning Regimens

New, less intense conditioning regimens are being used today that retain the desirable effects of standard high-dose conditioning regimens, but with significantly lower transplant-related mortality (TRM).

Non-myeloablative and reduced-intensity conditioning regimens have also expanded the number of patients eligible to receive hematopoietic cell transplants.

Non-Myeloablative Regimens

Non-myeloablative regimens use significantly lower doses of pre-transplant chemotherapy drugs and/or radiation than the traditional high-dose, myeloablative regimens that have been in use for more than 35 years. Non-myeloablative regimens do not attempt to completely eliminate malignant cells prior to transplant, but instead rely upon a graft-versus-malignancy effect mediated by donor-origin T cells. [1]

Non-myeloablative transplants have expanded the number of patients eligible for hematopoietic cell transplantation. Due to its lowered toxicity, non-myeloablative transplants can be appropriate for:

- Patients older than 55 years, which is a common upper limit for standard myeloablative transplantation
- Patients with one or more co-morbidities that would ordinarily exclude them from undergoing myeloablative transplantation

Although long-term follow-up data are not yet available, lower TRM and reduced rates of acute and chronic GVHD have been achieved in older patients and in patients with co-morbidities receiving non-myeloablative transplants, with rates comparable to those achieved by younger transplant patients. [2]

Clinical studies of non-myeloablative transplantation have shown that the graft-versus-malignancy effect is particularly pronounced in:

- Chronic myelogenous leukemia
- Chronic lymphocytic leukemia
- Low-grade, non-aggressive lymphomas [1]

Autologous transplant followed by non-myeloablative allogeneic transplantation is also being investigated by several groups. This treatment strategy attempts to combine the tumor cytoreduction of a high-dose autologous transplant with the lowered TRM of a non-myeloablative conditioning regimen with an allogeneic transplant. This technique has been particularly successful in treating patients with multiple myeloma. [3]

Reduced-Intensity Regimens

These regimens use combinations of chemotherapy drugs such as fludarabine, busulfan, ATG, and melphalan. They are not fully myeloablative, but they use higher doses than non-myeloablative regimens.

Initial reports have shown that reduced-intensity regimens have acceptable remission rates and lower overall rates of toxicity compared to standard high-dose therapy. [1,4] Rates of acute and chronic GVHD after reduced-intensity regimens are comparable to those observed in standard high-dose transplants, but the onset of GVHD is often delayed by weeks to months. [5]

Myeloablative Regimens

Despite the many successes in reducing the intensity of conditioning regimens, fully myeloablative regimens are still used for the majority of patients undergoing hematopoietic cell transplantation.

High-dose regimens are particularly useful in conditioning patients with aggressive malignancies, where there is a need for a strong anti-leukemia or anti-tumor effect.

Cyclophosphamide plus total body irradiation (TBI) and cyclophosphamide plus busulfan are typical approaches for fully myeloablative regimens, but combining busulfan with fludarabine is increasing in use. [6, 7]

References

1. Antin JH. Stem cell transplantation -- harnessing of graft-versus-malignancy. Curr Opin Hematol. 2003; 10(6):440-444. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14564175
2. Couriel DR, Saliba RM, Giralt S, et al. Acute and chronic graft-versus-host disease after ablative and nonmyeloablative conditioning for allogeneic hematopoietic transplantation. Biol Blood Marrow Transplant. 2004; 10(3):178-185. http://www.bbmt.org/scripts/om.dll/serve?action=searchDB&searchDBfor=art&artType=abs&id=as1083879103004191&nav=abs
3. Maloney DG, Molina AJ, Sahebi F, et al. Allografting with nonmyeloablative conditioning following cytoreductive autografts for the treatment of patients with multiple myeloma. Blood. 2003; 102(9):3447-3454. http://www.bloodjournal.org/cgi/content/abstract/102/9/3447
4. Alyea EP, Kim HT, Ho VT, et al. Comparative outcome of non-myeloablative and myeloablative allogeneic hematopoietic cell transplantation for patients greater than fifty years of age. Blood. E-print ahead of publication. Sept. 30, 2004. http://www.bloodjournal.org/cgi/content/abstract/2004-05-1947v1
5. Niederwieser D, Maris M, Shizuru JA, et al. Low-dose total body irradiation (TBI) and fludarabine followed by hematopoietic cell transplantation (HCT) from HLA-matched or mismatched unrelated donors and postgrafting immunosuppression with cyclosporine and mycophenolate mofetil (MMF) can induce durable complete chimerism and sustained remissions in patients with hematological diseases. Blood. 2003; 101(4):1620-1629. http://www.bloodjournal.org/cgi/content/full/101/4/1620
6. Kroger N, Zabelina T, Kruger W, et al. Comparison of total body irradiation vs busulfan in combination with cyclophosphamide as conditioning for unrelated stem cell transplantation in CML patients. Bone Marrow Transplant. 2001; 27(4):349-354. http://www.nature.com/cgi-taf/DynaPage.taf?file=/bmt/journal/v27/n4/abs/1702802a.html
7. De Lima M, Couriel D, Thall PF, et al. Once-daily intravenous busulfan and fludarabine: clinical and pharmacokinetic results of a myeloablative, reduced-toxicity conditioning regimen for allogeneic stem cell transplantation in AML and MDS. Blood. 2004; 104(3):857-864. http://www.bloodjournal.org/cgi/content/abstract/104/3/857

Last Updated: January 2005